REMARKS

Claims 1-15 are pending. In the Office Action dated March 22, 2004, the Examiner rejected claims 1-15 and requested a new title. The Examiner also withdrew the requirement for election of species as set forth in the Restriction Requirement dated May 19, 2003. In particular, the Examiner stated that the Applicants' argument that there would be no undue burden to search the nuclear hormone receptor superfamily was persuasive. Applicants thank the Examiner for the withdrawal of the election of species requirement.

Applicants have herein cancelled claims 1-15 and added claims 16-29. Support for the new claims may be found throughout the specification, e.g., at pages 2-4; 5 (lines 22-24); 6 (line 24) – 7 (line 1); 7 (lines 8-26); 9 (lines 11-14); 12 (lines 4-11); 13 (lines 14-25); 14 (lines 1-12); 14 (lines 20-26); 15 (Table 1); 16 (lines 1-26); 17 (lines 1-17 and Table 2); and 18 (lines 1-6). No new matter has been added. Accordingly, claims 16-29 are pending. Applicants have also amended the title to read: "Fluorescence Polarization Assays for Screening Binding of Ligands to Steroid Hormone Receptors."

In light of the amendments and remarks herein, Applicants respectfully request reconsideration and allowance of all claims.

Objection to the Specification

The Examiner requested a new title, asserting that the original title was not descriptive. Applicants have amended the title to read: "Fluorescence Polarization Assays for Screening Binding of Ligands to Steroid Hormone Receptors." Applicants respectfully submit that the new title is indicative of the invention to which the claims are directed, and request withdrawal of the objection.

Objection to the Information Disclosure Statement

The Examiner lined through Reference C16, asserting that it was not cited in the correct format. Applicants have provided a Supplemental IDS herein citing Reference C16 in the correct format. Applicants respectfully request withdrawal of the objection.

Rejections under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 12 and 13 as being indefinite. Applicants have cancelled claims 12 and 13 herein, and respectfully request withdrawal of the rejections as moot.

Rejections under 35 U.S.C. § 102(b)

The Examiner rejected claims 1-7, 10-12, and 14-15 under 35 U.S.C. § 102(b) as being anticipated by WO 98/05962 (Bolger *et al.*) (hereinafter "Bolger"). In particular, the Examiner stated that Bolger teaches a fluorescence polarization method for measuring the competitive binding of molecules to steroid hormone receptors; that ER may be used in the Bolger method; and that the Bolger methods can be carried out in multiwell formats.

Applicants respectfully disagree with respect to the present claims. A claim is anticipated under § 102(b) only if each and every limitation is disclosed in a single prior art reference. Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 639 (Fed. Cir. 1989) and MPEP § 2131. Present independent claims 16 and 17 are directed to methods for monitoring a binding interaction of a steroid hormone receptor (SHR) or a ligand binding domain (LBD) of a steroid hormone receptor, respectively, with a test ligand. The method includes

(a) contacting a fluorescently-labeled steroid hormone ligand with a steroid hormone receptor (or a ligand binding domain (LBD) of a steroid hormone receptor) where the steroid hormone receptor is selected from the group consisting of an androgen receptor (AR), a glucocorticoid receptor (GR), and a progesterone receptor (PR), to form a reference mixture;

(b) measuring the fluorescence polarization of the reference mixture;

(c) contacting the reference mixture with the test ligand to form a test mixture;

(d) measuring the fluorescence polarization of the test mixture; and

(e) comparing the fluorescence polarization of the reference mixture to the fluorescence polarization of the test mixture to determine if the test ligand competes with the fluorescently-labeled steroid hormone ligand for binding to the steroid hormone receptor (or LBD of the steroid hormone receptor).

At no point does the Bolger reference teach a method for monitoring a binding interaction of a steroid hormone receptor (SHR) or a ligand binding domain (LBD) of a steroid hormone receptor where the steroid hormone receptor is selected from the group consisting of an androgen receptor (AR), a glucocorticoid receptor (GR), or a progesterone receptor (PR). Accordingly, Bolger cannot anticipate the present claims, and Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b).

The Examiner also rejected claims 1-3, 5-6, 10-12, and 14-15 under 35 U.S.C. §102(b) as being anticipated by WO 99/27365 (Lustig *et al.*) (hereinafter "Lustig"). In particular, the Examiner stated that Lustig teaches a fluorescence polarization method of screening for modulators of nuclear hormone receptor function comprising measuring the "binding of a sensor polypeptide . . . to a nuclear hormone receptor in the presence of a candidate agent. The sensor comprises a peptide with a receptor binding sequence and a fluorescent label." (emphases added). The Examiner also stated that Lustig discloses the use of the method with the receptors LXR and ERR.

Applicants respectfully disagree with respect to the present claims. As indicated previously, independent claims 16 and 17 are directed to methods for monitoring a binding interaction of a steroid hormone receptor (SHR) or a ligand binding domain (LBD) of a steroid hormone receptor, respectively, with a test ligand. The method includes
(a) contacting a fluorescently-labeled steroid hormone ligand with a steroid hormone receptor (or a ligand binding domain (LBD) of a steroid hormone receptor) where the steroid hormone receptor is selected from the group consisting of the androgen receptor (AR), the glucocorticoid receptor (GR), and the progesterone receptor (PR).

At no point does the Lustig reference disclose a method for monitoring a binding interaction of a steroid hormone receptor (SHR) or a ligand binding domain (LBD) of a steroid hormone receptor where the steroid hormone receptor is selected from the group consisting of an androgen receptor (AR), a glucocorticoid receptor (GR), and a progesterone receptor (PR). Moreover, Lustig fails to teach the use of a fluorescently labeled steroid hormone ligand in his methods. Rather, all of the Lustig sensors include labeled peptides that bind as coactivators of

the nuclear hormone receptors (and thus not as steroid hormone ligands, as required by the present claims). Accordingly, Lustig does not anticipate the pending claims, and Applicants respectfully request withdrawal of the rejections.

Rejections under 35 U.S.C. § 103

The Examiner also rejected claims 1-12 and 14-15 under 35 U.S.C. § 103 as being unpatentable over Bolger in view of U.S. Patent No. 6,054,295 (hereinafter "the '295 patent"). In particular, the Examiner stated that Bolger did not teach fusion proteins of nuclear hormone receptors with GST, but that the '295 patent disclosed GST fusion constructs of full length nuclear hormone receptors and GST fusion constructs of nuclear hormone receptor ligand binding domains. The Examiner went on to state that it would have been obvious to include the fusion constructs of the '295 patent in the Bolger methods, as the motivation and expectation of success were disclosed in the use of the fusion proteins of the '295 patent to identify compounds that modulate wild type nuclear hormone receptors.

Applicants respectfully disagree. Proper analysis under § 103 requires consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition, and (2) whether the prior art would also have revealed that in so making, those of ordinary skill would have had a reasonable expectation of success. In re Vaeck, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

As indicated previously, the present claims are directed to methods for monitoring a binding interaction of a steroid hormone receptor (SHR) or a ligand binding domain (LBD) of a steroid hormone receptor with a test ligand. The method includes

(a) contacting a fluorescently-labeled steroid hormone ligand with a steroid hormone receptor (or a LBD of a steroid hormone receptor) where the steroid hormone receptor is selected from the group consisting of an androgen receptor (AR), a glucocorticoid receptor (GR), and a progesterone receptor (PR). As noted above, Bolger does not teach or suggest the present claims. The '295 patent does not cure the deficiencies of Bolger. At no point does the '295 patent teach or suggest that one having ordinary skill in the art should modify the methods of

Bolger to select AR, GR, or PR as the steroid hormone receptor for use in an FP assay. Furthermore, one having ordinary skill in the art would have had no reasonable expectation of success that GST fusion constructs of AR, GR, or PR could be successfully employed in the present methods given the '295 disclosure. The simple fact that the '295 patent discloses GST fusion constructs of nNR1, nNR2, or nNR2-1 for expression purposes provides no reasonable expectation of success that similar GST fusion constructs of AR, GR, or PR would function effectively in an FP assay for monitoring a binding interaction of a steroid hormone receptor (SHR) with a test ligand, as required by the present claims. Indeed, as one having ordinary skill in the art would recognize, ligand binding by a steroid hormone receptor can be greatly affected by numerous factors, including uncertain effects due to steric, charge, and conformational changes as a result of the addition of an N-terminal GST domain. Accordingly, the present claims are not obvious given Bolger in view of the '295 patent, and Applicants respectfully request withdrawal of the rejections.

CONCLUSION

Applicants submit that all claims are in condition for allowance, which action is requested. The Examiner is invited to telephone the undersigned if such would expedite prosecution. Enclosed is a $380.00 check (for $90.00 excess claims fee and a $290.00 multiple dependent claim fee), as well as a $950.00 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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